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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/593,417	06/14/2000	Raymond Andersen	108281-00001	8238
7590 03/03/2004				
Arent Fox Kintner Plotkin & Kahn PLLC 1050 Connecticut Avenue N W Suite 600 Washington, DC 20036-5339			EXAMINER LUKTON, DAVID	
			ART UNIT	PAPER NUMBER

1653

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/593,417

Applicant(s)

ANDERSEN ET AL.

Examiner

David Lukton

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 December 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4 and 8-13 is/are pending in the application.
- 4a) Of the above claim(s) 2-4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 8-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Pursuant to the directives of the amendment filed 12/24/03, claims 1-4 have been amended. Claims 1-4, 8-13 remain now pending.

Claims 2-4 remain withdrawn from consideration as being drawn to non-elected subject matter. The response filed 12/24/03 argues that there is a limitation that "should" be read into claims 2-4. This limitation is that when  $R_{71}$  is hydrogen,  $R_{70}$  is not hydrogen. The response further argues that claims 2-4 fall within the scope of claim 1. The examiner would agree that it is not the case that all embodiments of claims 2-4 fall outside the scope of claim 1. But claims 2-4 are quite ambiguous as to whether all of the embodiments (of claims 2-4) must fall within the scope of claim 1. A skilled organic chemist considering the language of claims 2-4 would perceive that  $R_{70}$  can be hydrogen, and at the same time,  $R_{71}$  can be hydrogen. There is nothing in the language of claim 2, 3 or 4 which would suggest that when  $R_{70}$  is hydrogen,  $R_{71}$  must be a substituent other than hydrogen, or that when  $R_{71}$  is hydrogen,  $R_{70}$  must be a substituent other than hydrogen. Thus, claims 2-4 permit  $R_{70}$  and  $R_{71}$  to simultaneously represent hydrogen. A reasonable interpretation of claims 2-4 would be that the possibility of  $R_{70}$  and  $R_{71}$  simultaneously representing hydrogen supercedes any limitation that claim 1 might impose on  $R_{70}$  or  $R_{71}$ . Accordingly, it is appropriate to regard claims 2-4 as a non-elected invention. However, in the event that each of claims 2-4 is amended to make clear that when  $R_{71}$  is hydrogen,  $R_{70}$

cannot be hydrogen, these non-elected claims will be rejoined for further examination.

Claims 1 and 8-13 are examined in this Office action.

Applicants' arguments filed 12/24/03 have been considered and found persuasive in part.

The rejection of claims 1 and 9 over Morriello ('250) is withdrawn.

\*

The response filed 12/24/03 argues that the examiner chose not to consider references "AI" or "AJ" [IDS (filed 10/30/02)], and that the examiner provided no reason for this decision. However, a reason was provided at the end of the previous Office action (mailed 8/27/03). To reiterate, the documents in question should be uniquely identified, and the year of publication should be included in the citation.

\*

Claims 1 and 8-13 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- There is a typographical error in claim 1 within the definition of variable R<sub>75</sub>.

Claim 1 recites the following:

"R<sub>75</sub> represents an optionally substituted alkyl group or Q'-COX, wherein Q' is an optionally substituted.... -CH<sub>2</sub>C/C- or...".

Here, the designation **-CH<sub>2</sub>C/C-** should instead depict an acetylene.

- Each of claims 10-12 is dependent on a non-elected claim

\*

The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by Huang (*J Am Chem Soc* **114**, 9390, 1992).

As indicated previously, Huang discloses (page 9400, col 1) the following peptide ("MeTrp" is *beta*-methyltryptophan):

Phe-Pro-Phe-MeTrp-Lys(Fmoc)-Thr

The explanation provided in the previous Office action was that claim 1 would be anticipated when the substituent variables correspond as follows:

R<sub>1</sub> = hydrogen

R<sub>2</sub> = hydrogen

R<sub>3</sub> = butyl substituted with fluorenylmethoxycarbonylamino

R<sub>6</sub> = substituted acyl (i.e., the tripeptide Phe-Pro-Phe)

R<sub>7</sub> = hydrogen

R<sub>70</sub> = methyl

R<sub>71</sub> = hydrogen  
R<sub>72</sub> = hydrogen  
R<sub>73</sub> = hydrogen  
R<sub>75</sub> = substituted alkyl  
n = zero

The response filed 12/24/03 has amended claim 1 to eliminate the possibility that R<sub>6</sub> can be substituted acyl. However, the claim still permits R<sub>6</sub> to be substituted alkyl. If an alkyl group is substituted with an oxo group, the result is again an acyl group. Thus, the only difference between a "substituted alkyl", and a "substituted acyl" is that in the case of "substituted alkyl", one additional substitution is required (i.e., substitution with oxo). And if claim 1 were amended to eliminate the possibility that R<sub>6</sub> can be substituted alkyl (in addition to having eliminating the possibility that R<sub>6</sub> can be substituted acyl), the claim would still be anticipated, since substituent variable R<sub>2</sub> can be substituted acyl or substituted alkyl.

The rejection is maintained.

\*

Claims 1 and 8 are rejected under 35 U.S.C. §102(a) as being anticipated by Talpir (*Tetrahedron Letters* **35**, 4453, 1994).

Talpir discloses a compound at the bottom of page 4456. This compound is specifically excluded from the scope of claim 1 for the case of "Y" being an unidentified substituent, i.e., the exclusion is for the case of integer variable "n" being zero. This

ground of rejection is directed at the case of substituent variable "Y" being hydrogen.

When substituent variable "Y" is hydrogen, integer variable "n" can be 1, 2, 3 or 4.

Accordingly, for the case of "Y" being hydrogen, and "n" being an integer other than zero, the claims are anticipated.

\*

Claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by O'Sullivan (USP 5,081,225).

O'Sullivan discloses (col 1, line 21+; col 1, line 33) the compound janthinocin C. This is a cyclic peptide which contains the amino acid dehydrotryptophan.

Claim 1 encompasses the possibility of  $R_{71}$  and  $R_{72}$  being "joined together such that a double bond is formed between the carbon atoms to which they are attached". When this double bond is formed, and at the same time,  $R_{70}$  is hydrogen, the result is dehydrotryptophan. As such, claim 1 encompasses any peptide that contains dehydrotryptophan. In claim 1,  $R_6$  can be an acyl group that is substituted with a peptide, and  $R_{75}$  can be  $-\text{CH}_2-\text{CONH}-R_{10}$ . Variable  $R_{10}$  can be substituted with anything, including a peptide. Even cyclic peptides would be included, because the terminal substituents (i.e.,  $R_6$  at the N-terminus, and  $R_{10}$  at the C-terminus) can be substituted with anything. Thus,  $R_6$  can be a group which is "substituted" with  $R_{10}$ , and  $R_{10}$  can be a group which is "substituted" with  $R_6$ .

Accordingly, the claim is anticipated.

✱

Claim 1 is rejected under 35 U.S.C. §102(b) as being anticipated by Minaev, V. E.  
("Fluorescence study of A-128-OP antibiotic", Deposited Doc. (1977), VINITI 2778-77)

Minaev discloses (page 9) the structure of a cyclic peptide which contains both dehydrotryptophan and methyltryptophan.

Peptides containing dehydrotryptophan are encompassed by claim 1, as are peptides containing methyltryptophan. The explanation given above in the rejection over O'Sullivan (USP '225) applies here as well.

Thus, the claim is anticipated.

✱

The following is a quotation of 35 USC §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention

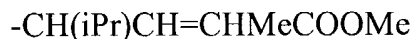


dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1, 8, 10-12 are rejected under 35 U.S.C. §103 as being unpatentable over Talpir (*Tetrahedron Letters* **35**, 4453, 1994).

Talpir discloses a compound at the bottom of page 4456. Also disclosed (page 4454) is that this compound was treated with diazomethane to afford the corresponding methyl ester. The methyl ester was also treated with acetic anhydride to afford N-acetylation of the secondary amino group. The reference does not provide explicit structures for the methyl ester or the N-acetyl compound.

In the case of the methyl ester, variable  $R_{75}$  would be the following (iPr = isopropyl):



This compound is not excluded by the proviso at the end of claim 1. If the claim were amended to exclude the methyl ester, the claim would still be rejected because  $R_2$  or  $R_6$  can represent an acetyl group.

Thus, the claim is rendered obvious.

\*

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Fromageot (U.S.P. 5,356,794).

Fromageot discloses a method of preparing peptides and proteins which contain

dehydrotryptophan. Specific peptide substrates are provided in table I (col 7, line 50+). Fromageot does not provide an explicit structure for any of the peptides containing dehydrotryptophan.

As indicated, Fromageot discloses a method of preparing peptides and proteins which contain dehydrotryptophan. Among the peptides in which the tryptophan was converted to dehydrotryptophan was the following [table I, col 7, line 50+]:

KKKHWVYYTCCPDTPYL

Letting  $P^1$  represent the tetrapeptide KKKH, and letting  $P^2$  represent the peptide YTCCPDTPYL, and letting " $\Delta$ Trp" represent dehydrotryptophan, the peptide resulting from the method of Fromageot would be the following:

$P^1$ - $\Delta$ Trp-Val-Tyr- $P^2$

Claim 1 encompasses any peptide containing dehydrotryptophan when  $R_{71}$  and  $R_{72}$  are "joined together such that a double bond is formed between the carbon atoms to which they are attached". The peptide  $P^1$ - $\Delta$ Trp-Val-Tyr- $P^2$  would be encompassed if the substituent variables correspond as follows:

$R_2$  or  $R_6$  is substituted with  $P^1$ ;

$R_3$  is alkyl

$R_{75}$  is  $-\text{CH}_2-\text{CONH}-R_{10}$  in which  $R_{10}$  is substituted with  $P^2$ ;

$Q'$  is substituted with the side chain of tyrosine.

Thus, the claim is rendered obvious.

✱

Claim 1 rejected under 35 U.S.C. §103 as being unpatentable over Minaev, V. E. ("Fluorescence study of A-128-OP antibiotic", Deposited Doc. (1977), VINITI 2778-77) in view of Minaev *Chem. Abstracts* 91:21053, 1979).

The structure disclosed in Minaev is indicated above. Based solely on the structure provided, a person unskilled in the Russian language could not determine that a second compound was prepared by cleaving the ester bond of the depicted structure. The *Chem Abstr.* citation, however, indicates that the ester bond of the cyclic peptide was cleaved, leading to an increase in the distance between the two indole groups (or at least an increase in the number of degrees of freedom). The open-chain peptide resulting from cleavage of the cyclic peptide of Minaev has been assigned registry number 70569-55-0 by *Chem. Abstracts*.

This peptide meets the limitations of two different embodiments of claim 1. First, the peptide is encompassed by claim 1 for the case of R<sup>70</sup> representing methyl and R<sup>71</sup> representing hydrogen. Second, the peptide is encompassed by claim 1 for the case of the amino acid containing the indole group representing dehydrotryptophan (as discussed above).

Serial No. 09/593,417  
Art Unit 1653

-11-

Thus, the claim is rendered obvious.

\*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at 571-272-0951. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*D. Lukton 2/27/04*

*Christopher S. F. Low*  
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